Table SI 1. Procurement details of SAMPL6 pK_a challenge compounds

SAMPL6 Molecule ID	Group	Supplier	LOT	CAT	Supplier reported purity	CAS	eMolecules ID	canonical isomeric SMILES	Experimental Molecule ID
SM01	fragment-like	AchemBlock	11549	10222	95%	521937-07-05	6679830	c1cc2c(cc1O)c3c(o2)C(=O)NCCC3	M01
SM02	fragment-like	ChemDiv	CM02432403	3232-0333			1327907	c1ccc2c(c1)c(ncn2)Nc3cccc(c3)C(F)(F)F	M02
SM03	fragment-like	ChemDiv		Z27474679			1228629	c1ccc(cc1)Cc2nnc(s2)NC(=O)c3cccs3	M03
SM04	fragment-like	ChemDiv		Z126957826			30719859	c1ccc2c(c1)c(ncn2)NCc3ccc(cc3)Cl	M04
SM05	fragment-like	ChemDiv		Z119335440			18908671	c1ccc(c(c1)NC(=O)c2ccc(o2)Cl)N3CCCCC3	M05
SM06	fragment-like	ChemDiv		Z28487401			18893169	c1cc2cccnc2c(c1)NC(=O)c3cc(cnc3)Br	M06
SM07	fragment-like	Enamine	2017-0168841	Z57161635	95%	100818-54-0	1327878	c1ccc(cc1)CNc2c3ccccc3ncn2	M07
SM08	fragment-like	Enamine	2017-0168838	Z57157353	95%	65418-08-8	1367649	Cc1ccc2c(c1)c(c(c(=O)[nH]2)CC(=O)O)c3ccccc3	M08
SM09	fragment-like	Enamine	2017-0168839	Z220564816	95%		1865544	COc1cccc(c1)Nc2c3ccccc3ncn2.Cl	M09
SM10	fragment-like	Enamine	2017-0168843	Z69130143	95%	35056-22-5	23354217	c1ccc(cc1)C(=O)NCC(=O)Nc2nc3ccccc3s2	M10
SM11	fragment-like	Maybridge	142989	RJC00689SC	90%	5334-30-5	719540	c1ccc(cc1)n2c3c(cn2)c(ncn3)N	M11
SM12	fragment-like	Maybridge	265423	DP00818SC			1859493	c1ccc2c(c1)c(ncn2)Nc3cccc(c3)Cl.Cl	M12
SM13	fragment-like	Maybridge	248841	GK03474SC			5828805	Cc1cccc(c1)Nc2c3cc(c(cc3ncn2)OC)OC	M13
SM14	fragment-like	Enamine		Z57290870			31653344	c1ccc(cc1)n2cnc3c2ccc(c3)N	M15
SM15	fragment-like	Enamine		Z1318268952			37095168	c1ccc2c(c1)ncn2c3ccc(cc3)O	M16
SM16	fragment-like	VitaScreen		STK098832			1284691	c1cc(c(c(c1)Cl)C(=O)Nc2ccncc2)Cl	M18
SM17	fragment-like	VitaScreen		STK032731			1444229	c1ccc(cc1)CSc2nnc(o2)c3ccncc3	M19
SM18	drug-like	Enamine		Z278071350			18897105	c1ccc2c(c1)c(=O)[nH]c(n2)CCC(=O)Nc3ncc(s3)Cc4ccc(c(c4)F)F	D01
SM19	drug-like	Enamine		Z30206127			3365457	CCOc1ccc2c(c1)sc(n2)NC(=O)Cc3ccc(c(c3)Cl)Cl	D02
SM20	drug-like	VitaScreen		STL282831			46568819	c1cc(cc(c1)OCc2ccc(cc2Cl)Cl)/C=C/3\C(=O)NC(=O)S3	D05
SM21	drug-like	VitaScreen		STL368658			1574612	c1cc(cc(c1)Br)Nc2c(cnc(n2)Nc3cccc(c3)Br)F	D06
SM22	drug-like	VitaScreen		STK070581			536848	c1cc2c(cc(c(c2nc1)O)I)I	D07
SM23	drug-like	VitaScreen		STK097966			4375254	CCOC(=O)c1ccc(cc1)Nc2cc(nc(n2)Nc3ccc(cc3)C(=O)OCC)C	D08
SM24	drug-like	VitaScreen		STK090644			1415746	COc1ccc(cc1)c2c3c(ncnc3oc2c4ccc(cc4)OC)NCCO	D09

Table SI 2. Calculated properties and descriptors of compounds of 28 compounds selected and procured for pKa challenge. pKa measurement experiments were successful 24 molecules labeled SM01-SM24.

SAMPL6 Molecule ID	Experimental Molecule ID	group	Epik pK_as in [3,11] range	OpenEye XlogP	Molecular Weight (g/mol)	eMolecules reported availability (mg)	Number of rotatable bonds	Number of UV-chr. units	eMolecules ID	canonical isomeric SMILES
SM01	M01	fragment-like	[9.119]	3.27	289.26	184	0	27	6679830	c1cc2c(cc1O)c3c(o2)C(=O)NCCC3
SM02	M02	fragment-like	[4.05]	3.61	301.39	101	3	36	1327907	c1ccc2c(c1)c(ncn2)Nc3cccc(c3)C(F)(F)F
SM03	M03	fragment-like	[7.12]	3.52	269.73	379	5	14	1228629	c1ccc(cc1)Cc2nnc(s2)NC(=O)c3cccs3
SM04	M04	fragment-like	[5.564]	3.79	304.77	415.5	3	36	30719859	c1ccc2c(c1)c(ncn2)NCc3ccc(cc3)Cl
SM05	M05	fragment-like	[5.346]	2.92	328.16	424.3	4	18	18908671	c1ccc(c(c1)NC(=O)c2ccc(o2)Cl)N3CCCCC3
SM06	M06	fragment-like	[4.001, 10.328]	2.91	235.28	406	3	37	18893169	c1cc2cccnc2c(c1)NC(=O)c3cc(cnc3)Br
SM07	M07	fragment-like	[5.564]	2.80	293.32	208.7	3	36	1327878	c1ccc(cc1)CNc2c3ccccc3ncn2
SM08	M08	fragment-like	[4.109]	3.14	287.74	232.1	3	59	1367649	Cc1ccc2c(c1)c(c(c(=O)[nH]2)CC(=O)O)c3ccccc3
SM09	M09	fragment-like	[4.05]	2.72	311.36	119.7	3	36	1865544	COc1cccc(c1)Nc2c3ccccc3ncn2.Cl
SM10	M10	fragment-like	[8.672]	1.50	211.22	149.1	6	28	23354217	c1ccc(cc1)C(=O)NCC(=O)Nc2nc3ccccc3s2
SM11	M11	fragment-like	[3.869]	3.90	292.16	3430	1	31	719540	c1ccc(cc1)n2c3c(cn2)c(ncn3)N
SM12	M12	fragment-like	[4.05]	2.60	295.34	7366	2	36	1859493	c1ccc2c(c1)c(ncn2)Nc3cccc(c3)Cl.Cl
SM13	M13	fragment-like	[4.267]	2.91	235.28	1864	4	36	5828805	Cc1cccc(c1)Nc2c3cc(c(cc3ncn2)OC)OC
-	M14	fragment-like	[5.564]	2.33	209.25	208.7	3	36	1327878	c1ccc(cc1)CNc2c3ccccc3ncn2
SM14	M15	fragment-like	[6.348]	2.22	210.23	50213	1	40	31653344	c1ccc(cc1)n2cnc3c2ccc(c3)N
SM15	M16	fragment-like	[5.82, 8.709]	4.23	263.33	21650.2	1	40	37095168	c1ccc2c(c1)ncn2c3ccc(cc3)O
-	M17	fragment-like	[3.158]	2.93	267.11	283.7	2	24	45809595	CC(C)c1ccc(cc1)/C=C\2/c3ccccc3NC2=O
SM16	M18	fragment-like	[4.714, 9.847]	3.31	269.32	385	3	20	1284691	c1cc(c(c(c1)Cl)C(=O)Nc2ccncc2)Cl
SM17	M19	fragment-like	[4.902]	3.34	426.44	170	4	30	1444229	c1ccc(cc1)CSc2nnc(o2)c3ccncc3
SM18	D01	drug-like	[9.381, 10.773]	5.17	381.28	247.7	7	37	18897105	c1ccc2c(c1)c(=O)[nH]c(n2)CCC(=O)Nc3ncc(s3)Cc4ccc(c(c4)F)F
SM19	D02	drug-like	[9.167]	5.78	403.31	489.9	6	28	3365457	CCOc1ccc2c(c1)sc(n2)NC(=O)Cc3ccc(c(c3)Cl)Cl
-	D03	drug-like	[4.113]	4.72	401.48	324.5	6	35	10794751	CC(C)(C)c1cc(n(n1)c2ccccc2)NC(=O)Nc3cccc(c3Cl)Cl
-	D04	drug-like	[3.199]	5.24	380.25	636.9	5	34	3064762	c1ccc(cc1)C(=O)Nc2ccc(cc2)Oc3c4c5c(sc4ncn3)CCCC5
SM20	D05	drug-like	[8.05]	4.14	438.09	154	4	24	46568819	c1cc(cc(c1)OCc2ccc(cc2Cl)Cl)/C=C/3\C(=O)NC(=O)S3
SM21	D06	drug-like	[3.892]	3.37	396.95	222	4	28	1574612	c1cc(cc(c1)Br)Nc2c(cnc(n2)Nc3cccc(c3)Br)F
SM22	D07	drug-like	[3.511, 6.794]	2.94	420.46	239	0	29	536848	c1cc2c(cc(c(c2nc1)O)I)I
SM23	D08	drug-like	[6.336]	2.79	391.42	319	10	28	4375254	CCOC(=O)c1ccc(cc1)Nc2cc(nc(n2)Nc3ccc(cc3)C(=O)OCC)C
SM24	D09	drug-like	[4.829]	3.27	289.26	398	7	71	1415746	COc1ccc(cc1)c2c3c(ncnc3oc2c4ccc(cc4)OC)NCCO